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Ohio Cardiovascular Health Collaborative

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# Cardi-OH ECHO Hypertension

Thursday, April 18, 2019

# Disclosure Statements

The following planners, speakers, moderators, and/or panelists of the CME activity have financial relationships with commercial interests to disclose:

- Adam T. Perzynski, PhD reports being co-founder of Global Health Metrics LLC, a Cleveland-based software company and royalty agreements for forthcoming books with Springer publishing and Taylor Francis publishing.
- Siran M. Koroukian, PhD reports ownership interests in American Renal Associates, and Research Investigator subcontract support from Celgene Corporation.
- George L. Bakris, MD reports partial salary from Bayer as FIDELIO PI, partial salary from Janssen as CREDENCE Steering Committee, partial salary from Vascular Dynamics as Calm-2 Steering Committee, and receiving honorarium as a consultant to Merck, NovoNordisk.
- Luke J. Laffin, MD reports being a member of the Hypertension Committee for the CALM-2 Trial of endovascular baroreceptor amplification (EVBA) procedure from Vascular Dynamics.
- These financial relationships are outside the presented work.

All other planners, speakers, moderators, and/or panelists of the CME activity have no financial relationships with commercial interests to disclose.

# Diagnosis and Evaluation of Secondary Hypertension


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# Objectives

- Define “secondary hypertension”.
- List the three most common causes of secondary hypertension.
- Describe the diagnostic evaluation of a patient with suspected renal disease or primary aldosteronism as a cause for hypertension.

# Epidemiology

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| TYPE | PREVALENCE |
|---|---|
| ESSENTIAL HTN | 90-95% |
| SECONDARY | |
| PRIMARY RENAL DISEASE<br>- **CKD**<br>- Urinary tract obstruction (ie Page Kidney)<br>- Renin producing tumor<br>- Liddle's | 3-6% |
| **RENOVASCULAR DISEASE** | 0.5-4.0% |
| **MEDS** | |
| **OBSTRUCTIVE SLEEP APNEA** | |
| ENDOCRINE<br>- **PRIMARY HYPERALDOSTERONSIM**<br>- HYPER/HYPO-TSH<br>- PHEOCHROMOYTOMA<br>- CONGENITAL ADRENAL HYPERPLASIA | 1-15% |

# Chronic Kidney Disease & Hypertension

- CKD patients 80-85% have HTN
  - Prevalence of HTN increase as CKD gets worse
- Pathogenesis
  - Na retention – degree of extracellular volume expansion may NOT lead to edema
  - Increase renin-angiotensin activity
  - Increased activity of sympathetic system
- Diuretics
  - Chlorthaldione has half life twice that of HCTZ
  - Use loop when GFR < 30
    - Lasix should be bid at least d/t short half life

# Chronic Kidney Disease & Hypertension- Treatment

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## Proteinuric CKD

First line - ACEi or ARB

- Blocks renin-angiotensin axis
- Reduces proteinuria
- Slows progression of CKD
- Combo ACEi/ARB (or ARB/DRI) can reduce proteinuria more so than mono therapy but not generally recommended
  - In DM combo does not improve renal outcomes and increase risk of AKI, hospitalization, and hyperK
  - Does not provide additive effect on BP
- Second line – diuretics
  - Enhances anti-HTN and anti-proteinuric effect of ACEi/ARB

## Nonproteinuric CKD

First line

- No specific benefit to any particular drug class
- If edematous – start with diuretic

# Renovascular Hypertension

- Pathogenesis of HTN similar to that in CKD
  - Na retention
  - Activation of renin-angiotensin system

- Etiology
  - ASD > 2/3 of cases
  - FMD the rest

# Whom to Re-Vascularize

- FMD revascularization improves BP in 60-80%
- ASD revascularization improves BP < 50%
  - Patients with large vessel ASD likely have small vessel ASD
  - Several RCT's have found no benefit of revascularization compared to medical therapy
    - ASTRAL
    - CORAL
  - Selection bias in RCT's
    - Observational studies have generally shown benefit to revascularization
  - Criteria for revascularization in ASD
    - Progressive ischemic CKD
    - Failure of optimal medical therapy (or intolerance)
    - Short duration of HTN
    - Recurrent flash pulm edema or refractory CHF

# Diagnosis

- Patient selection is critical
  - Diagnostic testing for RVD is not indicated unless patient meets criteria for revascularization
    - Optimize medications before proceeding w/ evaluation
      - ACEi/ARB +/- diuretics most likely to be effective
      - May result in rising sCr but that in of itself does not warrant discontinuation

- Specific testing
  - Duplex – Cheap and non-invasive but technically difficult and operator dependent
  - CTA – Good sensitivity and specificity but requires dye load
  - MRA – Good sensitivity and specificity. May or may not require gadolinium
  - Captopril renogram – Reasonable specificity but poor sensistivities – misses a lot of patients that would respond to revascularization
  - Plasma renin – Poor sensitivity and specificity

# Obstructive Sleep Apnea

- Patients with OSA more likely to have HTN than non-OSA
  - 50% of OSA patients have HTN
- Patients with resistant HTN often have OSA
  - 75% of resistant HTN patients have OSA
- Treatment of OSA results in improvement in BP
  - Effect of CPAP is minor but significant (2-3mmHg)
  - Those with excessive daytime sleepiness or very severe OSA tend to have more pronounced improvement in BP
  - Most trials have looked at CPAP but other devices do seem to help

# Drug-Induced Hypertension: Prescription Medications

- Steroids
- Estrogens
- NSAIDS
- Phenylpropanolamines
- Cyclosporine/tacrolimus
- Erythropoietin
- Sibutramine
- Methylphenidate
- Ergotamine
- Ketamine
- Desflurane
- Carbamazepine
- Bromocryptine
- Metoclopramide
- Antidepressants
  - Venlafaxine
- Buspirone
- Clonidine

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# Primary Hyperaldosteronism

- Rarer cause of secondary HTN but concerns re “sub-clinical” PH
  - Variable prevalence noted in literature anywhere from 4-13% in primary care and up to 30% in referral centers
  - Aldactone added as second line therapy in JNC 8 guidelines
- Classic triad
  - HTN
  - HypoK
  - Metabolic alkalosis
- HypoK not consistent
  - Renal K wasting requires high sodium intake and elevated aldosterone levels
  - Diuretic induced hypoK may represent PH

# Diagnosis

- Serum aldosterone and renin
  - Renin should be suppressed with high aldosterone level
  - Criteria
    - ALDO/RENIN > 20 + ALDO > 25 is diagnostic
    - Levels are dependent on sodium intake and posture and may vary minute to minute
    - RENIN < 1.0 raises concern for suppressed renin
      - ACEi/ARB and diuretics lead to elevated renin levels – suppressed renin in these settings very suggestive of PH
- Salt loading 24hr
  - High sodium intake will suppress normal aldosterone secretion
  - Measure Na and aldo on high salt diet → if Na > 200 and aldo > 12 then PH

# Treatment

## Medical therapy

- Mineralcorticoid agonists
  - Dose titrated to normokalemia
  - Aldactone
    - Long-acting
    - Numerous AE
    - Inexpensive
  - Inspra
    - Short-acting
    - Less side effects
    - Expensive
- BP will improve over weeks so de-escalate meds slowly
- Expect increase in sCr after initiation

## Surgical therapy

- Unilateral disease in 30-40%
- Adrenal vein sampling - Indicated in all pts considering surgery and are surgical candidates except
  - Age < 40 and unilateral adenoma
  - Adrenal carcinoma or large adenoma > 5cm
- De-escalate meds immediately after surgery
  - Stop MRA
  - Stop all hyperK inducing meds

# PH Outcomes

## Surgery versus Medical therapy

- Historical data suggest patients with PH have more CVD than non-PH independent of BP
  - Adrenalectomy for those eligible has been treatment of choice
- Recent data suggest if renin unsuppressed that outcomes similar to general population

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# Thank you!

# Questions/Discussion